Chapter 1

Introduction

Q1. "There is no safety in numbers, or in anything else."
James Thurber (1939).

Q2. "Often before now have I applied my thoughts to the puzzling question – one, probably, which will puzzle me for ever – why it is that, while all Greece lies under the same sky and all the Greeks are educated alike, it has befallen us to have characters so variously constituted."
Theophrastus (371-287 BCE; [1]).

Q3. **"**Already at the age of twenty-five you see the professional mannerism settling down on the young commercial traveler, on the young doctor, on the young minister, on the young counselor-at-law. You see the little lines of cleavage running through the character, the tricks of thought, the prejudices, the ways of the 'shop,' in a word, from which the man can by-and-by no more escape than his coat sleeve can suddenly fall into a new set of folds. In most of us, by the age of thirty, the character has set like plaster, and will never soften again."
William James (1890, *p*. 79 [2]).

Q4. "Neuroticism scores reflect a person's characteristic (or mean) level of distress over a protracted period of time. In this perspective, even prospective associations of neuroticism with mental health outcomes are basically futile, and largely tautological since scores on any characteristic with substantial within-subject stability will predict, by definition, that characteristic and related variables at later points in time. Neuroticism is not an explanatory concept in the aetiology of psychopathology, since it measures a person's characteristic level of distress over a protracted period of time. This situation will not change until knowledge becomes available about: (i) the mechanisms that produce high neuroticism scores (and, therefore, also psychopathology) and (ii) its neurobiological substrate. Only then will we understand why neuroticism appears to 'predict' the outcomes it predicts."
Hans Ormel (2004, [3]).

Q5. "Personality is the supreme realization of the innate idiosyncrasy of a living being. It is an act of courage flung in the face of life, the absolute affirmation of all that constitutes the individual, the most successful adaptation to the universal conditions of existence, coupled with the greatest possible freedom of self-determination"
Carl Jung (1875-1961).

Q6. "Traits are not behaviour. They are summary statements describing likelihood of and rates of change in behaviour in response to particular situational cues. In addition to their relationship to the probability and latency of a response, stable predispositions may be conceptualized in terms of differential sensitivities to situations and differential response rates".
William Revelle (1995, [4]).

Q7. "Give me a dozen healthy infants, well-formed, and my own specified world to bring them up in and I'll guarantee to take any one at random and train him to become any type of specialist I might select – doctor, lawyer, artist, merchant-chief and, yes, even beggar-man and thief, regardless of his talents, penchants, tendencies, abilities, vocations, and race of his ancestors. I am going beyond my facts and I admit it, but so have the advocates of the contrary and they have been doing it for many thousands of years".
John B. Watson (1930, [5]).

OUTLINE OF THE THESIS

Behaviour is that what an organism does over the course of a lifetime in response to internal and external signals, such as environmental influences [6-8][1]. Organisms navigate the landscape of life in predictable, variable, and quantifiable different ways, both relative to (i) conspecifics under similar environmental conditions and (ii) in terms of differences in stability or change of traits in changing environments [9-15][2]. One salient way in which individuals differ is their personality, the coherent patterns of affects, goals, cognitions, and behaviors they show over time and space - the things we feel, think, want, and do [16-22]. The backbone of personality captures individual differences in sensitivity, reactivity, flexibility, and responsiveness to environmental stimuli, a cross-species phenomenon called 'emotionality' [12,13,22-26]. Most differences in sensitivity to environments and adaptability to novelty in humans is captured by the personality trait neuroticism [27-41].

At the broadest hierarchical level of human personality neuroticism is conventionally accompanied by four other broad trait domains: extraversion, openness to experience, agreeableness, and conscientiousness [16,18,20,42-51][3], a taxonomy that is called

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1. Welcome reader. The footnotes in this manuscript give specific references, supportive information, elaborations, or personal notes, which some readers may experience as "non-essential sideways". They can henceforth ignore them.
2. Personality traits refer to confined suits of cognitive-behavioral traits that vary consistently amongst individuals, but are maintained through time and across context [10,13,18,22,191]. For example, every animal differs in terms of boldness, aggressiveness, activity level, cooperativeness, fearfulness, dispersal or exploration tendencies, docility, impulsivity, sociability, or responsiveness to environmental stimuli [9,12,13,22,1124,1125]. Individual differences in personality are often large while intra-individual changes tend to be small, in comparison [15,23,145,1124-1126]. Allport introduced and defined traits in 1936 as "generalized and personalized determining tendencies – consistent and stable modes of an individual's adjustment to his environment" [131]. Behavioral ecologists call these consistent individual differences in behavior alternatively temperaments, personality differences, behavioral syndromes, or coping styles [12,15,1127]. The psychological realm is often divided over three levels of focus, *viz*. every individual is in certain respects (a) alike all other individuals, (b) like some other individuals, (c) and like no other individual, and the individual differences approach in personality captures this second level of description [16,20].
3. **Extraversion** refers to the tendency to have a positive outlook on life, to be sociable and risk taking, and to be orientated (or interested and energetic) towards the outer world of people and things rather than the inner world of subjective experience. The **Openness** to experiences or Intellect domain captures novelty seeking, curiosity, imaginativeness, creativity, and interest in cultural and educational experiences. Individuals high on openness tend to be willing to take risks as opposed to being narrow-minded and cautious (notably, openness should not be confused with self-disclosure). **Agreeableness** describes concern and sensitivity towards others and their needs, and high scores reflect the tendency to act in a cooperative, pleasant, and unselfish manner (likability). Very agreeable individuals get along well with others, but low scores refer to individuals who are antagonistic, mistrustful, unsympathetic, uncooperative, and rude, but probably good as a drill sergeant or bill collector [189]. **Conscientiousness** taps into organization, *viz*. high scorers are socially reliable, careful, scrupulous, and persistent in pursuing goals, and tend to be organized, responsible, and hardworking. But this focused deliberation at the high pole is matched by rashness and lack of organization at the low pole [643]. Interestingly,

the Big Five or Five Factor Model (FFM). All people can be ranked or ordered by the degree to which they manifest these traits. Henceforth I am only concerned with neuroticism, the single most important risk factor in behavioral public health [52-54], of which the top 25% high scorers generate total excess economic costs that exceed those of all the common mental disorders combined [55][4]. Neuroticism refers to the tendency to perceive the world as threatening, to be prone to experience unpleasant and disturbing emotions in reaction to various types of stress (emotional instability), and to select oneself into situations that foster negative affect [46,50,51,56-63]. Importantly, neuroticism is predictive for mental and physical health, mating success, mortality [64-69], subjective wellbeing [70-75], occupational attainment, divorce-risk, and wealth, and is often more predictive than current socioeconomic status or intelligence [65-69,76-80].

Twin studies indicate that about half of the individual differences in neuroticism can be explained by non-genetic factors [81-93]. In this thesis I will explore which environmental influences account for change in neuroticism, and how long such changes persists. Remarkably little is known about the environmental embedding of neuroticism levels [54,94,95], or how neuroticism changes as a consequence of environmental input [78,96-98], or via which pathways neuroticism has its detrimental effects [52,53,76,99,100]. Below the reader will be familiarized with i) the concept of neuroticism, ii) the idea of stability and change in neuroticism, iii) temperamental negative emotionality (*viz.*, fear and frustration), which is conventionally regarded to be a developmental precursor of adult neuroticism, iv) environment influences on neuroticism, and v) the concept of mutual reciprocity between neuroticism and stressful life events (SLEs), which is known as the corresponsive principle.

I will conclude with an outline of the position of neuroticism in the field of psychiatry, to emphasize the importance of dissecting environmental influences on stability and change in neuroticism. However, in the interest of suspense, I first outline the position of neuroticism in the psychological realm, structured in terms of the classic FFM of personality, a taxonomy that currently dominates the field [16,20,46,101,102].

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conscientiousness also assesses the extent to which individuals consider future consequences of possible actions. However, different personality theorists define personality differently, often based upon their theoretical positions [17]. Conventionally 3 to 16 higher-order personality traits are distinguished, depending on the organizational framework or taxonomy [16,17,20].

4. And approximately two-thirds of the costs of the somatic disorders per million inhabitants [55].

PSYCHOLOGICAL TRAITS

Psychological traits are heuristics to describe characteristic ways in which individuals are different or alike, or how individuals respond to specific environmental influences [16,105]. The psychological realm has historically been subdivided over *characteristic adaptations* which are traits that are learned or otherwise acquired and *basic tendencies* which are traits that have a biological (often heritable) basis [46,97,101][5], as outlined in Figure 1. Basic tendencies capture inborn *abilities* such as intelligence, empathy, or musical and verbal abilities [20,106-109], and personality *dispositions* like neuroticism [16,46,101][6]. Dispositions like neuroticism (N, depicted at the right in Figure 1, in grey) are deemed to manifest themselves indirectly, via behaviours and characteristic adaptations, such as the skills and beliefs depicted in Figure 1 [16,22,101,102,105,110-112].

Characteristic adaptations refer to culturally conditioned phenomena such as goal strivings, attitudes, feelings, thoughts, behaviors, needs, drives, and desires, that are thought to be relatively consistent across situations (within individuals), but to differ over generations and around the world [16,24,101,110,111,113,114]. Allport famously defined personality as "the dynamic organization *within the individual* of those psychophysical traits that determine his unique adjustments to his environment" [115]. In other words, characteristic adaptations are the typical outcomes of transactions between neuroticism and specific environmental influences at particular points in development. From this perspective differences in how neuroticism manifests itself across contexts do not impede a common underlying mechanism.

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5. Aristotle (384–322 before the common era, or BCE) argued that character (traits) and habit (behaviour) were reciprocally related [128,1128], a foundational assumption in modern personality theory [16,17,20]. Socrates wondered how people could experience two mental states at the same time, *e.g.* commit a crime or desire something, and being simultaneously averse to it, which seemed impossible within an unified soul [1129]. Plato solved this problem with a tripartite theory of the soul (or psyche), which held that each soul was composed of three distinct but intangible parts (a logical, spirited, and appetitive sphere), in analogy of the three castes in each society Plato had imagined in his treatise the Republic [1130]: cognition (*cf.* the intellect of the philosopher kings), affect (*cf.* the emotions of the soldiers), and desire (*cf.* the will of the workers, merchants, and docters) [1130]. These three core (latent) constructs still form the basic structure of the psycholical realm [108,299,1129-1132]. From the city-soul parallel also a theory of the mind emerged, *viz.* when our actions were governed by reason our soul was in balance (psychic harmony, *cf.* Kallopolis, the excellent city), but four kinds of unjust balances could disarrange the soul, *e.g.* emotions rule (timocracy), reason rules (oligarchy), our appetitive forces rule (democracy), and only one faculty remains (tyranny) [1130].
6. Personality traits (*viz.*, thoughts, feelings, behaviors) and cognitive abilities are indeed among the most stable psychological characteristics [99,106,164,165,1133]. This concept of stability refers to the degree to which the relative differences between individuals are preserved over time (called differential stability), which is usually assessed with test-retest correlations, and discussed in chapters 4, 5 and 10.

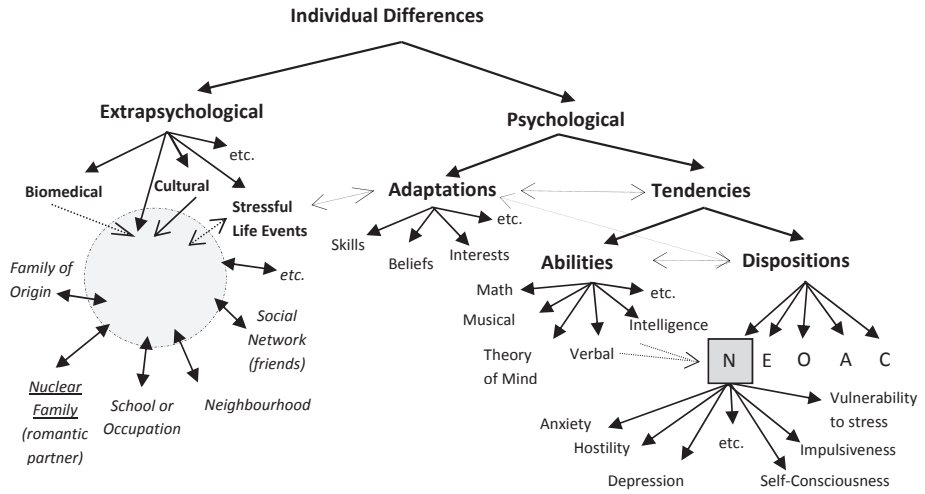

Figure 1 The Position of Neuroticism in a Hierarchical Taxonomy of Individual Difference Variables based on Five Factor Theory and Ecological Systems Theory.

Note. The left section of the figure is based on Bronfenbrenner's Bioecological Systems Theory [103,104] and shows an individual Mesosystem and a nested suit of Microsystems that together capture the environment that an individual inhabits. The right section is based on the Five Factor Theory (see [46,101]), and shows the Five Factors of personality: N= Neuroticism, E= Extraversion, O= Openness, A= Agreeableness, C= Conscientiousness. The figure has been adapted with permission from "the Place of the FFM in Personality Psychology" ([45], *p*.59).

NEUROTICISM

Neuroticism is generally conceived as a latent entity (from the Latin latēre, which means 'to lie hidden') that manifests itself indirectly and also exists when its behavioral expression is currently absent [16,17,20,116-118][7]. Each individual has a charac-

7. Plato outlined in 380 BCE that 'forms' or souls were nonphysical conceptual realities that captured the true "essence" of a material reality, but lay beyond the ordinary range of human understanding, thus were latent [1134]. This idea became eternalized in Plato's "Allegory of the Cave" metaphor in which prisoners chained in a dark cave since childhood interpreted shadowns cast on the wall in front of them as their world with moving figures, rather than in terms of the objects themselves behind them, which cast the shadow (their 'essences') [1130]. This concept echoes in the premise that personality traits are biologically determined 'essences' that do not change in response to environmental factors. This led to the idea that dispositions manifest themselves indirect via characteristic adaptations and to the distinction between observed scores and latent (true) scores [17,105,407]. The way neuroticism manifests itself in daily behavior can be observed in experience-sampling studies [110,392] and in how individuals express themselves on blogs and social media [140,141,1049], see Figure 2. High neuroticism is presumed to be (a) internal in the sense that humans carry this disposition across contexts and (b) causal because it explains behavior of the individual who possesses it [16,119,1114]. However, note that individuals high on frustration-proneness who do not encounter triggers to activate this propensity shall not show frustration [123,195]; similarly, someone high on extraversion may be rather silent and sad after the loss of a loved one; and a tendency to take charge may be inhibited in social situations

teristic mean level of neuroticism, but all people vary around this mean under different circumstances, which leads to a density distribution of negative feelings [94,114,119]. The higher we score on neuroticism, the more likely we are to show the behavior it disposes towards. Moreover, all individuals vary in different degrees on neuroticism, with leads to a distribution that approximates a normal curve.

Neuroticism is a 'latent' reference for a network of rather heterogeneous affective, cognitive, and behavioral personality components, which in the FFM framework are subdivided over six lower-order facets [16,47,119]. Each facet captures emotions that we all experience from time to time, but we differ in the frequency and intensity with which we experience these feelings. The *Anxiety* facet captures the level of free floating anxiety and proneness to fear. *Angry hostility* measures the tendency to experience anger, frustration and bitterness. *Depression* indicates a tendency to experience feelings of guilt, sadness, loneliness, and hopelessness. *Self-consciousness* is a measure of how prone people are to shame or embarrassment, and refers to feelings of inferiority to others, often manifest as shyness or social anxiety. *Impulsiveness* describes the tendency to act on cravings and temptations rather than delaying gratification, which manifests in a tendency to overeat, overspend, to drink, smoke, gamble, and use drugs. Finally, *Vulnerability* describes individuals' general susceptibility to stress, which results in panic in emergencies and a dependence on others for help. However, high neuroticism scores typically refer to high scores on all traits, which is a substantial personal (and societal) burden [53,54,119]. Nevertheless, some individuals can be anxious but not hostile, or impulsive but not self-conscious.

The nature of the relationship between neuroticism and its manifestations remains a topic of debate [102,116,117][8]. The FFM perspective holds that neuroticism *causes* its underlying cognitive, affective, and behavioral 'personality components' to vary and interact [16,101,102,110,111]. The alternative perspective is to see the spectrum of personality that hitherto has been identified as a *descriptive* summary of average levels of trait-relevant actions, which implies that the covariation among facets still requires a causal explanation [16,17,102,117][9].

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which have an identified leader [16,1135]. The manifestation of personality can thus differ across individuals, over time, and within individuals across situations, *e.g.* one individual with high openness to experience may frequently change from occupation (but maintain a stable romantic relationship) while others may engage in several intime relationships over the life course (but keep the same job).

8. Some theorists take the many asociations between traits to suggest that a comprehensible number of latent factors accounts for much of the variation in personality structure [111,1136]. FFM theorists propose that *proximal* causes, which refers to the manifested 'source' or outer traits - the observable aspects of neuroticism - are *qualitatively* distinct from *distal* causes, which refer to the latent inner trait, which is deemed to manifest itself indirectly [102,137,1137]. The empirical support is not impressive [1138].
9. Many theorists convey that personality psychology lacks a grand theory that explains the forces that underlay individual differences [16,17,24,24,76,102,110,111,116,1136,1139,1140]. There is currently

In sum, neuroticism is thought to manifest itself in many behaviors, cognitions, emotions, perceptions, skills, beliefs, life goals, narrative identities, how they change, of what they consist, how they lead to outcomes, and how they are formed in the first place [18,19,24,32,46,76,101,102,120-125]. Different individuals can therefore perceive even identical environmental influences rather differently, and will not show the same symptoms and signs. Now neuroticism has been put in position in the psychological realm, and I outlined that neuroticism is multidimensional (*viz*. every individual has a unique mix of facet scores that jointly result in neuroticism scores), we can explore neuroticism as a broad trait domain.

A Short History of Neuroticism

The study of individual differences and stability or change in neuroticism has a long tradition [17,126,127][10]. However, the modern concept of neuroticism as a dimensional

no explanation available in terms of a neurocognitive, evolutionary, or functional theory beyond general notions of traits as calibrations to serve as effective means to desired ends [24,1092,1105,1135,1141]. Some theorists argue that anxiety, anger, frustration, or jealousy, may well have a situational rather than dispositional cause, in keeping with the situationalist tradition [8,16,102,117,149,698,867]. Though it is often argued to be rather embarrassing that we do not understand the internal workings of traits [76], theorists can also be surprisingly resistant against functional explanations for human personality [22,24,1135], while there is little doubt that chimpanzees flexibly adjust their behavior to maximize payoffs [1142,1143].

10. The Egyptian Ebers Papyrus, written by the physician Imhotep, is with 3500 years the oldest source on psychiatry. Imhotep believed that negative emotions like anger or sadness could cause 'diseases of the hearth', such as disturbances of emotions, thinking, intellect, and behavior, and psychotic and mental symptoms [1144]. Hysteria was due to 'starvation' or upward wandering of the womb, who could be lured down with sweet-smelling substances on the genitals, or driven up by eating foul-smelling or tasting substances [1144]. Such attribution of agency to non-human objects is called "animism", and typical for hunter-gatherer tribes, who tend to live in an enchanted worlds in which all natural phenomena possess a personality, from prey animal to rainbows [1145-1147]. When Egyptians mummified their death (human or animal) they scooped out their brains (and threw them away), but carefully preserved the hearth, which was the tangible form of the mind that was needed during future incarnations [1004]. About 2800 years ago, at the dawn of Classical Antiquity, most people believed that the psyche or soul was inborn in all animals alike, who shared their origin and emotions, which seated in the heart or gut [17,1148]. The soul was a material attribute that became destroyed by dispersion when a body died, a phenomenon that was associated with widespread worries [1129]. A soul was seen as a natural force that drove changes in the physical world, *e.g*. the soul of a seedling accounted for its potential to grow into a tree, processes we nowadays frame in terms of genetic inheritance [22,1149]. Because the soul was conceived as a material attribute the relation between body and soul was not a point of discussion [1129]. Humans were thought to have differentiated themselves from animals over time when they had established rulers, laws, crafts, and cities [17,1148]. Madness came from the gods as a spiritual punishment for sin and disobedience [17,1027]. Plato invented the immaterial soul to give the mortal body a natural opposite (*cf*. hot-cold, asleep and awake), which must be immortal and indestructible, thus pre-existed somewhere with 'the anima mundi' (world soul or heavens) before it came down to Earth to join a material body [17,1129]. Plato believed that after death our souls resonated with spirits 'dispatched by the world soul' [17,1131], reminiscent of ancestral spirits in animistic hunter-gatherer cultures [1147,1150], and the "vitalistic" forces that caused health and physical disease in Egyptian and Mesopotamian theories [17]. Hippocrates (470 to 370 BCE) theorized that these "vitalistic" forces were physiologically expressed as balances between four bodily fluids or humours, based upon the

personality domain emerged in the first half of the 20th century [16,17,20,128,129], when the invention of factor analyses enabled theorists to condensate the about 20.000 trait indicators in natural language into comprehensive trait taxonomies [17,119,130,131][11]. In the 1940s Hans Eysenck coined the cluster of emotional instability and maladjustment 'neuroticism', because Eysenck felt that the associated behaviors were most clearly seen in individuals who were diagnosed with neurosis [17,119,130,131][12].

four basic elements in nature that the Greeks observed: blood (air), black bile (earth), yellow bile (fire), and phlegm (water) [17,683,1151]. Galen of Pergamum (200-130 BCE) popularized the idea that four mixes (or "temperaments") of these humours resulted in a typical imbalance, reflected in a **sanguine**, **choleric**, **melancholic**, or **phlegmatic** personality type [123,1151]. Melancholy referred to a propensity to be mentally unbalanced, fearful, anxious, or sad, thus a conceptual predecessor of neuroticism, which was attributed to an overabundance of black bile [123,683]. This temperamental humor theory remained the dominant proto-scientific personality theory for 1500 years [123,1151] until in the 19th century Wilhelm Wundt and William James transformed humour theory into a dimensional trait concept that incorporated the principle of a fixed internal milieu: a setpoint with homeostasis [17,94,128,135,1152]. Much of current personality terminology echoes humour theory, *e.g.* state of mind, temper, and mood [17,1153].

11. Aristotle and Theopastrus created the first lists of personality traits about 2400 years ago, but the field remained stagnant because of a general inaptitude to create a sensible structure for the huge amount of personality indicator and failure to identify dimensions of commonality [16,17,20,128]. Additionally, early generations lacked statistical techniques to analyze the data, proved unable to collect data systematically, and failed to develop testable theories [17,128]. Francis Galton ignited the 'statistical enlightenment' in the 1870s with the invention of the concept of a statistical scale, multivariate analysis [1154,1155], and his discovery of his 'index of co-relation' in 1888 [1154] and 'reversion to the mean' [105]; refined into the Pearson product-moment correlation coefficient or '*r*' by his student Karl Pearson (1857-1936) [17,1154]. Galton's breakthrough enabled Charles Spearman and Louis Thurstone to elaborate correlations into a tool to associate multiple variables [17,1156]. This multiple-correlation enabled personality theorists to assort thousands of trait-variables into groups ('dimensions') of high affinity theorized to share a core, a method called 'factor analysis'. Galton's methodological advancements and studies of twins also gave birth to quantitative genetics [17,1157], see chapter 9. In addition, Galton invented the chi-square test for a normal approximation of discrete data [1122], which forms the foundation for a comparison of structural equation models in chapter 3 and 6. In sum, modern personality psychology emerged about three generations ago with the invention of correlation, regression, and factor analysis [17,20].
12. Until the 17th century physicians used horoscopes to judge how the stars and planets affected the humours (bodily fluids) of patients to diagnose mental illness [1131]. In the 17th century Thomas Willis rejected the idea that temperament or psychopathology were linked to a single body fluid or humour, and attributed hysterical, melancholic, and hypochondriac states to differences in neural functioning [1158,1159], which revived the brain as the center of personality [1158]. In 1769 the Scottish doctor William Cullen coined "Neurosis", the Greek word for 'nerve' with the suffix -osis for 'diseased or abnormal condition', to refer to a group of "disorders of sense and motion" caused by "a general affection of the nervous system" [17,126]. Platonian dualism (spirit versus body) echoes in the structure of medicine in which brain based problems or disorders (as reflected in neuropathological findings) became the domain of neurology while mind based problems (those without any demonstrable anatomical basis) became the domain of psychiatry [17,310]. Neurosis became indicative for a syndrome of nerve diseases without any demonstrable anatomical basis [126], which formed the core of psychoanalytic theory [17]. Neurosis was deleted from the DSM in 1980 because the DSM taskforce considered neurosis to be vague and unscientific [162]. However, the International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10) from the World Health Organization (WHO) still comprises a category of 'neurotic, stress-related and somatoform disorders' (code F40-F48), including specified (F48.8) and non-specified neurotic disorder (F48.9), or Neurosis NOS.

Eysenck defined neuroticism as the tendency to arouse quickly and to inhibit slowly [132,133], or 'affect intensity' [134,135]. However, other definitions have been formulated, *e.g.* Fiske defined neuroticism as emotional control or emotional maturity [136]; Catell defined neuroticism as anxiety [137]; Tellegen defined neuroticism as negative emotionality [58]; and Costa and McCrea conceptualized neuroticism as a dimension that runs from low-neurotic emotional stability or adaptability (calm and relaxed) to neurotic emotional instability and maladjustment [138,139]. Despite their different definitions theorists agreed upon many shared characteristics of neuroticism. In general, individuals scoring low on neuroticism are characterized by emotional stability and predictability, *viz.,* the tendency to be even-tempered without rapid changes in mood. Individuals high on neuroticism tend to be reactive, distressed, tense, and moody, as Figure 2 (page 18) illustrates colorfully.

Emotional Stability

Emotional stable individuals tend to feel secure, confident, calm, and feel able to adapt to novel situations, including the ability to 'bounce back' after negative experiences [17,18,46,142][13]. Emotional stability is common among alpinists [143,144], and extreme low scores are associated with increased risk behaviors [99,143,145], and psychopathic fearlessness [146,147][14]. Though emotional stable individuals are relatively free from negative affect, this does not equal more positive affect, which is primarily predicted by the trait extraversion [21,71,148-153], also prospectively [154,155]. Nevertheless, emotional stability seems most predictive for overall subjective wellbeing

13. Emotional stability has been characterized as a 'win-stay position', because individuals with adaptive or 'favourable' characteristics shall experience less need to change [123,250,329]. However, emotional stable individuals reared in religious families are less likely to be religious in adulthood than their neurotic peers [546,1160], which suggests that emotional stable individuals may change more in specific other domains. What is true, however, is that emotional stability appears to be a protective trait [158], predictive for resilience and the ability to maintain a stable equilibrium [1161], which Tineke Oldehinkel coined 'bouncability'. Neuroticism is not associated with positive feelings in pleasant situations, but in slightly unpleasant situations emotional stable individuals feel more positive than individuals high on neuroticism do [151]. Extraversion predicts most variance in positive experiences [21,71,152,153]. Notably, the association between neuroticism and negative affect is based on the assumption that the basic affective tone is positive [1162]. Deviations from this basic positivity (instability) may mainly be induced by negative experiences or circumstances that cause negative affect [1162]. Positive and negative experiences seem to activate basic evolutionary systems and to be (partly) processed in different brain areas [22,150].
14. Courage is not the absence of fear, but the judgment that something else is more important, thus resistance or mastery of fear (Mark Twain). Also Scott Stossel argued in "My Age of Aniety" that lack of anxiety and heroism are not the same [182]. Most animals feel intuitive fear in new circumstances when there is no past experience to validate (the intuition may be accurate, or may be not), but persistent unwarranted fears are manifestations of "neuroses" [22,149], nowadays framed as an anxiety disorder in humans [639,1109].

Figure 2. Characteristic Differences in Word Use in Social Media For Individuals Scoring High (Upper Panel) or Low (lower Panel) on Neuroticism.

Note. Figure is reprinted with permission from H. Andrew Schwartz and colleagues (2013, [140]). The Figure is based on an open vocabulary analyses of 700 million words, phrases, and topics collected from Facebook messages of 71,968 volunteers, here stratified by neuroticism (adjusted for age and gender, Bonferroni-corrected, $p < .001$ [140]). Neuroticism was measured with items from the International Personality Item Pool (IPIP, with a test-retest reliability >.80 [141]), a proxy for the NEO Personality Inventory Revised (NEO-PI-R) [47,119].

[70,75], and this effect increases with age [74,75,99][15]. Finally, emotional stability or stability of moods is universally in the top three of most valued mate (selection) characteristics [156-159][16], for both genders [159], even more uniform as for intelligence [160]. Multiple studies showed that individuals who try to make a good impression show more emotional stability [17,161][17], because unpredictability is generally considered to be a negative personality feature [17,162]. Over the lifespan individuals tend to become more emotional stable, and neuroticism decreases on average almost d= 0.80 between age 10 to 40 [163-165].

Neurotic Volatility

The high pole of neuroticism is characterized by emotional volatility, and feelings of anxiety, distress, depression, tension, vulnerability, as well as proneness for guilt and frustration, being easily frightened, and insecure in relationships with others [17,18,46,142]. Individuals high on neuroticism have unusually persistent emotional reactions, tend to focus on criticism and negative input, and are therefore often in a bad mood [36,54,62,94,166]. These negative emotions are accompanied by a perception of the environment as dangerous and beliefs about one's inability to control or cope with future challenges (vulnerability).

This process is often referred to as "falling apart" under stress [18,54,56,62,167], *e.g.* manifest in cognitive and somatic symptoms before an exam [168,169]. High neuroticism is generally associated with somatic symptoms [170-176], but also with many non-behavioral phenotypic variation [13,177-180][18], and fluctuating self-esteem

15. The correlation between emotional stability and subjective wellbeing was r= .22 in a meta-analysis of 74 studies [70]. It has been shown that emotional stability also predicts more variance in subjective wellbeing than extraversion does (38% *vs*. 23%, [1163]; 28% *vs*. 16% [1164]). Emotional stability associates best with items for individual wellbeing, whereas extraversion associates best with social items [1164]. Emotional stability and psychological wellbeing are also associated along the lifespan, whereas extraversion seems unrelated in samples younger than age 30 [1164]. Moreover, the inverse relationship between neuroticism and emotional wellbeing also becomes stronger with age [74,75].
16. Together with love and a dependable character [156,157,1165]. In cultures with more gender difference women value emotional stability and dependability even more than men [157]. This may be so because it reliably signals that resources will be provided consistently over time, thus can be allocated more efficiently to overcome the adaptive hurdles one encounters over a life [156]. Low neuroticism or emotional stability reflects resilience, *i.e.* an ability to cope with stresses and set-backs. If low neuroticism increases reproductive success it will spread at the expense of anything that does not, even if it would threaten survival [7].
17. Moreover, when acting in a neurotic fashion individuals report a greater sense of being abnormal or not fitting in with one's peers, and this feeling increases with age [250], possibly due to an increasing 'positivity effect' in older peers [206].
18. For example, lower physical muscularity [177,1078], more body weight [177-179], lower peak energy expenditure and aerobic capacity [180], a child-like face [1078], less self-assured posture [1078], faster motor decline with age [1166], lower telomere length [1079], hypertension [1167], and inflammatory cytokine (interleukin-6 [1080]), among others. Because high neuroticism is also a risk factor for the development of many somatic problems [52-55,171,172,176,688] it has been argued that high neuroti-

[149,181,182]. High neuroticism is characterized by the tendency to avoid risks, *e.g.* in sports [145] or with regard to finances [183], and is therefore often described in terms of a social threat detection system [31,41][19] or a 'better-safe-than-sorry strategy' that reduces the risk of losing at the price of limiting the chances of winning [145,184][20].

If you score high on neuroticism (thus are emotional volatile) it's not all doom and gloom, and some effects seem even beneficial under certain circumstances. For example, there are indications that synergistic effects with high conscientiousness can result in good health behaviours [99,185,186][21]. Furthermore, negative affect prevends risk-taking behaviour [187], *e.g.* one study showed that young adolescents who scored high on neuroticism at age 13 had a six times lower chance to die from accidents before age 25 [186][22]. Moreover, anxious individuals often end up better educated and with better jobs than very happy people tend to do [184,188].

Individuals high on neuroticism tend to be critical of themselves and their performances and are easily dissatisfied, which may propel self-improvement, which makes them proficient in environments that require critical thinking and evaluation, as they may put forth more effort to come up with creative ideas [189,190][23]. In its mild form, neurotic perfectionism provides the energy that leads to great accomplishments [149,190]. However, being extremely tough on themselves, they do not spare others. And over time people with a high level of neuroticism tend to find new reasons to complain, worry, and to be dissatisfied. Now we familiarized ourselves with the characteristics of neuroticism we focus on change in neuroticism.

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cism reflects a fitness indicator that signals mutation load [78,158,1107,1168,1169]. This would be in keeping with the sexual attractiveness of emotional stability [156,160].

19. For example, high neuroticism is closely tied to jealousy, which is a cognitive-emotional motivational complex that is often activated to channel attention in order to preserve key-resources, such as valued relationships [1170-1172].
20. High neuroticism indeed predicts higher speed and duration of orientation to threat [1173] and difficulty disengaging attention from sources of threat [1174].
21. Being nervous and worried while simultaneously being more conscientious provides a context for neuroticism to have a positive effect on health [185].
22. High neuroticism may theoretically exist for such survival benefits during childhood/adolescence alone [98,191].
23. Furthermore, individuals high on neuroticism also sober group decision making, often play devil's advocate, and point out all negative aspects of a proposal, which prevents groupthink [124,189]. It is also true that neurotics tend to set unrealistic high goals, which they often fail, which can lead to insecurity and self-defeat, and workaholicism [149,190]. Relationships with neurotic men – either self-rated, spouse-rated and interviewer rated - are costly because they tend to be self-centered, monopolize shared resources (and time), show higher than average sexual jealousy, are dependent, and tend to be both verbally and physically abusive [78,156]. Moreover, individuals high on neuroticism tend to have more affairs than average [476,481], which is a further diversion of time and resources [156].

Temperamental Negative Emotionality

Modern system theory contents that development consists of hierarchically organized characteristics that incorporate earlier emerging ones [25,98,191,192]. The limited array of basic temperamental traits that are displayed during infancy and early childhood form the building blocks of the later developing adult personality configuration [192-196]. Our temperament may be metaphorized as a hard ball of ice around which the softer snow of personality accumulates developmentally [197][24]. The exact temperamental traits that account for all individual variety are still debated, but most theorists distinguish three higher-order temperament traits: Positive emotionality, negative emotionality, and effortful control [18,123,198].

In this thesis we focused on negative emotionality, because this domain is often seen as the temperamental seed-form of adult neuroticism [18,22,123][25]. Negative emotions refer to sadness, fear, irritability and frustration, avoidance tendencies, and difficulty to

24. Substantial individual differences in reactivity and self-regulation are evident from the second trimester of gestation onwards [1175-1177], and have lawful implications for later development and differences in personality [18,192,1178]. During all developmental periods some children differ in their activity, shyness, and experience of emotions and distress [18,192,198,1179]. Temperaments have been defined as children's emotions and their susceptibility to them [123,198]. Others use a more broad definition in which temperaments capture all individual differences in affect, activity, attention, and self-regulation [18,123]. The difference between both definitions lays in the incorporation of traits that develop during the second year of life, such as the ability for effortful regulation of emotions and behavior, which are often regarded as cognitive rather than basic-emotional [18,123,124,1180], thus more familiar to abilities in the terminology of Figure 1 [18,98,1181]. For example, Walter Mischel's famous marshmallow experiment showed that the ability to delay gratification in four-year-olds produce simportant benefits into adulthood [1181]. But dispositions and abilities are closely related [209-213], *e.g.* motivational (dispositional) factors are strongly predictive for performance on intelligence tests [106,587,1182]. Gordon Allport [1183] defined temperament as "the characteristic phenomena of an individual's emotional nature, including his susceptibility to emotional stimulation, his customary strength and speed of response, the quality of his prevailing mood, these phenomena being regarded as dependent upon constitutional make-up and, therefore, largely hereditary in origin" [198,1183]. Such individual differences in functioning affect us daily, and shape who we are, who we become, what we experience, and how we behave, think, and live [16,21,98,123,192,195].
25. Temperamental negative emotionality encompasses two separate dimensions: emotional reactivity and emotion regulation [123,895,1184-1186]. Both dimensions have been associated with individual differences in motivational systems regarding sensitivity to reward and punishment [22,54,198]. Emotional reactivity (*cf.* emotionality, neuroticism, or distress) refers to the reactive component of an emotion ("arousal"), the excitability of motor or attentional responses, and orientation to internal and external environments [22,123,192]. Historically the emotional reactivity domain has been subdivided into two complement clusters: an "aggressive negative-affectivity to threat" pole, with active and approach-orientated emotions (such as anger, frustration, and hostility), associated with the externalizing domain of psychopathology [54,123,200,689]. A complement "non-aggressive negative-reactivity to treat pole" refers to less active and more avoidance-oriented emotions (such as anxiety, depression, fear, worry, guilt, dependency, and feelings of self-consciousness), which are closest related to the internalizing domain of psychopathology [54,123,200]. Adjustment is the result of both emotional reactivity and the child's abilities to regulate the expression of negative emotions (effortful control) over development [123,196,196,909,1187-1189]. More explicitly, emotional reactivity may not be a risk for externalizing problems when individuals exhibit executive control abilities strong enough to modulate the reactivity, in which case the child is able to respond in a flexible, adaptive, and socially acceptable way [909].

be quieted after high arousal [18,22,123,198]. More specifically, we focus on the emotional reactivity subdomain of negative emotional temperament, often operationalized as individual differences in the thresholds of reaction, latency, intensity, peak-intensity, duration, and recovery of negative affects/emotions, while the emotional regulation subdomain precedes adult conscientiousness [18,22,123,192,199].

When children navigate from infancy to late childhood (age 8-11) their temperaments become increasingly diversified, individuated, hierarchically integrated, and often more effective and stable [17,19,60,164,192,200-202]. Both positive and negative affects seem to become more distinct [74,192,203-206]. Most personality trait differentiation takes place between age 12 and 18, when our early emerging temperamental differences elaborate into human personality traits [19,207-209]. Trait differentiation is driven by increases in children's motor, cognitive, emotional, and language abilities, and individuals who are cognitively and verbally more able also show most trait differentiation [209-213]. These developments influence how we organize our behaviour, meet environmental demands, overcome challenges, and navigate our worlds [16,18,208].

It has been noted that correlational patterns between the Big Five traits are roughly comparable across samples of children and adults [208,214], but the cognitive maturity (verbal comprehension) that is required for most fine-grained and differentiated personality self-descriptions is only derived during early adolescence [16,192,208,209]. Aspects of personality that go beyond our emotional temperamental core include social cognition and self-related perceptions (*e.g.*, self-esteem or paranoia); social emotions like pride, guilt or shame [149,215,216]; the content of thoughts, attitudes, values, beliefs, morals, needs and goals; cognitive coping strategies and defence mechanisms; links between one's self and other entities in concepts, schemas, and life narratives; and cognitive adaptations to the social world [16,18-20,123,142,193,198,217], among other processes.

In sum, personality traits differ from basic temperaments in that their full structure emerges close to adulthood and is primarily moulded by the environment in which the individual is born, educated, and raised, thus experience and enculturation [16,17,218][26]. Temperamental negative emotionality is a developmental precursor of adult neuroticism and primarily manifested as fear and frustration over childhood [219,220] and as frustration in adolescence [219,220]. Now the normative development of neuroticism has been outlined, we focus on experience-driven within-individual change in neuroticism.

It is rather the combination of high emotional reactivity (high neuroticism) with low levels of self-regulation that is associated with the aetiology of child psychopathology [18,196].

26. The construction of life narratives, which vary in emotional tone, themes, and narrative complexity, are also fundamental aspects of personality traits like neuroticism [19,1190-1193]. Narrative identities subsume tasks, goals, projects, tactics, defenses, values, and other developmental, motivational, and/or strategic concerns that contextualize individual lives in time, place, and social roles [19,1190-1193].

THE MIXED MODEL OF CHANGE IN NEUROTICISM

The concept of neuroticism was first mentioned by the Roman orator Cicero (106-43 BCE), who, after he lost his daughter Tullia in childbed, was stunned by grief. Cicero wrote a treatise in which he distinguished this state of emotional reactivity or 'Angor' from an inborn disposition to be anxious and emotional reactive or 'Anxietas' [17,54,221]. Henceforth neuroticism referred to a person characteristic setpoint or average of a personal density distribution of negative mood states, which fluctuate dynamically in response to positive and negative experiences around this setpoint level [94,100,110,222,223][27]. The idea that most changes after major events result in short-term state fluctuations (episodes) in neuroticism, but that the neuroticism setpoint itself can change as well, given enough change in the environment, is called the mixed model of change in neuroticism (see chapter 2-4, [94]).

Nowadays most personality theorists acknowledge that personality is a mutable phenomenon, but at the dawn of the 21th century prominent theorists argued that the neuroticism setpoint (averages) became "fixed like plaster" between age 21 and 30 [2,119,224,225], after William James [2,226][28]. However, as outlined, each birth cohort undergoes a normative developmental decrease in neuroticism between age 10 and 45 of about d= 0.80 [163,227-229]. Moreover, many individuals show additional non-normative intra-individual changes in their neuroticism setpoint over the ebb and flow of life, given enough change in their surroundings [75,163,230-233]. This is nothing new, given that all pioneers of personality psychology argued that personality dispositions changed (*cf*. Galton, Catell, Allport, and Murray [17,127,164]).

THE ENVIRONMENT

The genetic influences on the neuroticism setpoint are rather stable and approach unity near age 30, while environmental influences become increasingly stable over adolescence and adulthood and plateau around age 45 [18,85,91,93,234-238]. Studies of identical twin pairs reared together and apart indicate that about half of the variance in neuroticism can be explained by non-genetic differences [81-92], which account for a substantial part of both stability and change in the neuroticism setpoint

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27. The setpoint refers to a desired (ideal normal value) in an internal regulatory system (*cf*. homeostasis), and we follow the Random House Dictionary (2014) and cybernetic convention and use setpoint rather than the set point in tennis.
28. This fixed like plaster perspective (see page 8 quote 3) can be seen as an "anachronism" from the past generation [228,1194].

[75,85,92,223,239][29]. These observations indicate that neuroticism should not be studied in a vacuum. Up to now theorists have been engrossed with the study of genetic predictors for both stability and change in neuroticism [83-85,88,91,172,240-242], but it seems at least equally important to try and chart and dissect environmental influences on neuroticism [75,93,235,243-247][30].

Many changes in neuroticism seem propelled by stressful person-environment transactions [18,92,93,246-248], including stressful social events [246,249], social roles, preferences, goals, cognitions [24,250,251], affects and biases [124,125], and selection, reactance, and evocation processes [18,24,252], as shall be outlined throughout this thesis. To me it seems more surprising how *stable* individuals tend to be in neuroticism [253], given the numerous events and role transitions humans tend to experience over life [93,99,163,164,249,253,254]. Neuroticism is a cognitive-behavioral complex that elaborates and differentiates over life, and in this thesis I focus on environmental influences that can account for changes in neuroticism.

The environment literally refers to the aggregate of all surrounding factors, things, conditions, or external influences that affect a given individual at a given time [7,25,96,248,255,256], but can also be understood as an insulating layer [25,103]. Because environmental influences can only be measured *relative* to genes, they tend to be quantified as the sum of all non-inherited phenotypic variance, which includes measurement error [93,257], intra- and inter-organismic influences, and prenatal factors [258,259]. The contribution of neuroticism to observable behaviour is often overshadowed by the press of circumstances. Personality traits account for about 10% of the individual differences in actual behavior in any specific instance [47,243], but personality traits are interesting because they indicate how people act in *general*, which means that neuroticism refers to our average behaviors across many instances.

Personality expression is most consistent within environments that are highly structured by social norms (cultural scripts, rituals, rules, expectations) or instincts, because in these situations most humans react similar, *e.g.* when in grave danger, at funer-

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29. Note that heritability estimates only refer to *actualized* genetic potential for neuroticism [103,475,547]. Genetically identical twin fetuses, which are virtually mirrored developmental programs that also develop in almost identical environments, can still grow up to be remarkably different [259,336,431,1175,1176]. In other words, identical twins can develop differently neuroticism levels (multifinality) while individuals with different starting conditions can derive at the same end result (equifinality) via different developmental pathways [93,195,310,1195]. If we picture neuroticism in terms of covered trait space, then genes form the length of the rectangle, while nurture forms its width, and each rectangle requires both [7,25,93,255].
30. For example, a study of Palestinian childen showed that the peace treaty between Israel and the PLO (Palestine Liberation Organization) led to an average reduction in neuroticism of d= 1.12 between January 1993 and 1994 [1196].

als, under strong social pressure, or in front of red traffic lights [96,260,261,261][31]. Personality differences reveal them most clearly in environments that are relatively free and unscripted (ambiguous), thus leave room for a wide range of adaptive responses (see Figure 1); *e.g.* when you are at home, with friends, in your occupational setting, after you experienced a stressful event, or in front of orange traffic lights [16,18,21,25,95,103,248,249,255,256,261-263][32]. In the family system a broader range of behaviors are allowed than in the occupational system [27,103,227].

The available evidence suggests that measures of the environment can be as stable as personality [24,25,103,248,262]. However, many life situations and social networks change over the lifespan, both in terms of the intimacy of the bonds that link individuals (*e.g.,* friend, partner, parent, employee), but also in the type of arenas in which the social interactions are played out [17,103,249,264]. To understand neuroticism, life situations must be described, measured, and taxonomized [100,244,245], and different situation taxonomies have been proposed over the years, but none has achieved widespread acceptance [103,245,265-267]. Similarly, there is no consensus on the optimal way to measure stressful experiences [268-271].

NEUROTICISM IN PSYCHIATRY

Finally, I explore the position of neuroticism in the field of psychiatry, to emphasize the general desirability of studying predictors for stability and change in neuroticism. In terms of the manual of mental disorders (DSM) from the American Psychiatric

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31. Strong social pressures can be illustrated with three famous psychological experiments that exemplify the power of situations. The Asch conformity experiment showed in the 1950s that about 75% of the participants changed their opinions (about the length of lines) towards those of the majority group, even though the majority was clearly wrong [1197,1198]. In the 1960s the Milgram obedience (or shock) experiment showed that about 70% of the participants inflicted *fatal* voltages on other participants to obey an authority figure who instructed them to perform acts conflicting with their personal conscience [1199]. Finally, the Stanford Prison experiment showed in the 1970s that a division of a group of participating students over guards (placed in a position of power) and prisoners (who had no control) led within six days to dehumanizing situations: guards behaved aggressive and abusive while prisoners grew passive and depressed (in these six days five prisoners had already been released because of severe negative emotions including crying and acute anxiety [1200]). While personality theorists sought to explain behavior by personality, social psychologists focused on situations (*cf.* the person-situation debate), but this divide has now been supplanted by research on dynamic person-environment transactions [245,249,1201].
32. Individuals may also display different aspects of her/his personality in different groups [17,195], in different languages [218,1202,1203], and in different situations [20,731], and individuals seem to differ more in a social context than when they are alone [1204]. Moreover, there are striking differences in both public and private expressions of emotions around the world [662,1205]. Furthermore, extraverted individuals have a greater positive impact on their social environment, but are also more likely to drive fast, to get into car accidents, and to commit more traffic offences in general [16,1206].

Association (APA)[33], neuroticism predicts both the common mental disorders (CMDs, *viz*. anxiety, depression, and substance use disorders, previous axis I), personality disorders (axis II), and their inter- and intra-axial comorbidity [3,52,53,149,272-283]. Neuroticism forms the core of the emotional flagship disorders [53,54,222,281,284-291][34], especially major depressive disorder or MDD [292-295][35] and anxiety disorders [54,296-299][36]. Neuroticism also shares most of their genetic roots [88,274,293-295,300-303][37]. These facts may not surprise, given that neuroticism and many interviews for psychiatric distress share multiple items [3,94].

From the perspective of Dutch society it is notable that about a million Dutch individuals took an antidepressant over the past year, and about two million a benzodiazepine [304,305]. This casts up to 10% of the adult population between age 15 and 65 [304,306][38]. Moreover, each year about 25% of the Dutch population is eligible for a psychiatric (DSM) diagnosis, and up to 50% of the population experiences such a

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33. The diagnostic and statistical manual of mental disorders, or DSM, is a dictionary that provides a common language and standardized criteria for the classification of mental disorders. Since the first edition in 1952 the DSM became a dictionary for clinicians, researchers, pharmaceutical drug companies, health insurance companies, the legal system, and policy makers [162,307]. Since May 2013 the fifth edition is available with up to 400 discrete disorders, lowered thresholds, and many non-specific symptoms [639].
34. See the tripartite model [284], with negative-affect/neuroticism as a non-specific general factor of emotional distress common to both anxiety and depression [3,53,54,290,1021], or associations between neuroticism/ negative-emotionality and the general factor of psychopathology [166,1030,1056].
35. MDD is manifested by about a fifth of all humans at some point in their lives [1207,1208], and also known to be sensitive to specific life experiences [628,840,1070,1070,1209-1211]. Criteria for a MDD diagnosis in the DSM-IV are two weeks of depressed mood and decreased interest or pleasure in daily activities, impaired function (social, occupational, educational), significant weight change (5%), and three of the following symptoms nearly every day: change in sleep, change in activity, fatigue or loss of energy, guilt/worthlessness, concentration problems, or suicidality [639]. Estimates of recurrence of MDD have been estimated to range from 33% to 70% within several years [322,774,1212].
36. Anxiety disorders make up the majority of lifetime mental health disorders worldwide [290,1213], and are known to be sensitive to environmental factors [872,1109,1214,1215]. Neuroticism is especially implicated in social anxiety, agoraphobia, and animal phobias [1216-1219], but neuroticism also predicts schizophrenia [748,1220], and shows substantial genetic overlap with schizotypy [280]. Schizophrenia is also related to environmental factors [1027,1221]. Generalized anxiety is defined in the DSM as a six-month period of uncontrollable worry accompanied by three or more persistent problems: restlessness, fatigue, concentration issues, irritability, muscle tension, or "sleep disturbance" [639].
37. For example, about half of the genetic variance in neuroticism and lifetime anxiety and mood disorders showed overlap in a twin study (n= 9000 [293]), and the genetic roots of neuroticism and general anxiety disorders overlap for 80% [301,1222]. Other studies report associations between the genetic roots of neuroticism and major depression (axis I) of r= .50 [274,295], and r= .37 for positive schizotypy (axis II) [280].
38. Women twice as often as men [304,306]. Notably, despite these drugs 75% of these individuals drive their car, which is a criminal offense in case of an accident [306]. The U.S. Food and Drug Administration has placed a 'black box' warning label on all antidepressant medications: the most serious type of warning for adverse side-effects [162].

period during their lifetime [307-309][39]. About half of all these mental diagnoses occur in individuals with a lifetime history of three or more diagnoses [162,308], which are probably based upon shared patterns of symptomatology, and known to cause significant impairment in school, work or social functioning [116,310].

Despite this burden, there is not a single reliable biomarker or biological test for any of the common psychiatric disorders [162,307,311,312][40]. There are no genes uncovered of even moderate effect size for any of the major psychiatric disorders [116,311], nor for personality [313-317][41]. There are no clear structural brain pathologies associated with mental disorders [307,318][42], and there are no convincing empirical data to support the current discrete diagnostic DSM-5 system [116,307,310,319-322]. This may suggest a mismatch between disease biology and how psychiatric diseases are categorized [162,311,321,323].

The psychotropic interventions that are currently available to psychiatrists tend to have small effects, about $d = 0.30$ [307,324,325][43], which is comparable to that of most non-psychotropic treatments [305,307,326]; and only half of the patients experience a

39. This led some theorists to question the validity of the diagnostic and statistical manual (DSM), with its discrete concepts, neglect of inter-individual variability, comorbidity (or symptom inter-correlation), and individual fluctuation [116,162,307,310,1223,1224]. Many authors argue that psychiatry nibbles at the edges of "normal" by classifying behaviors, thoughts, and feelings that once were regarded innocent (albeit perhaps somewhat weird or odd) as pathological, broadening the definition of mental illness [162,307,1224]. Nevertheless, about 15-20% of the Dutch population also reported one or more psychotic-like experiences [1027,1225], which suggests that many psychiatric symptoms are quite common.
40. Despite countless investigations into serotonin or other neurotransmitters there is still no method to cure clinical depression. In contrast, many pharmaceutical companies shut down their research into psychiatric drugs in this decade because, as they note, there is a lack of science providing good molecular targets for drug development [312,323]. This suggests that even the drug companies are moving away from the chemical-imbalance story [162,307].
41. Genome-wide Association Studies (GWAS) indicate that common single-nucleotide polymorphisms (SNPs) explain only about 6% (SE= 3%) of the phenotypic variance for neuroticism [989]. Similar findings have been reported for Cloninger's harm-avoidance scale [1226]. Hitherto there is neither a clear chromosomal marker [315,989] nor a (specific) gene for neuroticism that explains at least 1% of the genetic variance [315,790,989,1227,1228]. Our understanding of the genetic origins of personality trait variation is extremely limited [315-317,453] and genetic expression is also sensitive to strictly environmental conditions [25,453,1229]. It may be that gene-environment correlation [29,1230] is "the elephant in the room of the study of social behavior" [441,453], *viz*. something about the (genetically influenced) way people behave evokes responses from the environment that reinforce the genetic influences on that behavior (see chapter 3, 4, 9, and 10).
42. There are no clear differences in brain volume, concentration, cortical thickness, and surface, between individuals high versus low in neuroticism, *viz*. some researchers observed small differences (*e.g.*, [1231-1234]) but many others could not replicate these findings (*e.g.*, [1235-1237]). Albeit some report differences in functional connectivity [1115], strong claims on the biological basis of neuroticism are hitherto unjustified, due to inconsistencies and lack of replication, methodological limitations, and neuroticism's heterogeneity [238,1117].
43. These effects of about $d = 0.30 \pm 0.10$ are similar for depression, general anxiety disorder, panic, post-traumatic stress, or compulsions [307,324,325]. Such observations do not support the plethora of DSM labels [162,307].

clinically meaningful reduction in symptoms (up to full remission) due to medication, at least for the most common conditions [305,307,327]. Moreover, the therapeutic mechanisms behind these approaches remain largely unknown, and seem rather non-specific [305,307,312]. In short, both the pathophysiology and aetiology of the mental disorders we currently distinguish remain elusive, and we have few (reliable) tools to treat them, in spite of a century of intensive and costly research [162,307,323][44]. The central position of neuroticism in most CMDs (common mental disorders), in their comorbidity, and the substantive prospective association between neuroticism and CMDs has been a major drive behind the study of stability and change in the neuroticism domain.

Finally, though personality and mental disorders are currently studied in distinct and non-overlapping literatures, historically the concepts were united in the broad rubric of individual differences [17,20,77]. Probably both fields merge again in the future [76,77,196,281]. Until that point in time neuroticism is of great interest in its own right, as shall be outlined throughout this thesis. The major drive behind this thesis is our aim to learn to eventually target the vulnerability for emotional disorders inherent in high neuroticism, rather than its subsequent (clinical) manifestations.

AIMS AND OUTLINE OF THE THESIS

In the introduction I outlined that neuroticism is the single most important risk factor in behavioural public health, and paradoxically both one of the most stable and changeable personality traits as well. In the following I introduce the empirical studies that I performed to study environmental influences that predict change in neuroticism and the temporal dynamics of this change.

Chapter 2: Positive and Negative Experiences Predict Change in Neuroticism

In this chapter I study change in neuroticism in The Netherlands Study of Depression and Anxiety (NESDA, n= 2881, mean age at baseline= 42). I report about the overlap of change in neuroticism and anxiety and depression in reaction to stressful life experiences (SLEs) that occurred between baseline (T_1) and follow-up (T_2), and test four hypotheses:

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44. In other words, theorists may have ideas about how some things work in psychiatry, it remains difficult to overestimate how little we actually know. There must be a lawful relation between assemblies of neurons and the elements of thought, but we are currently at a loss to describe those laws. Science is clearly harder to apply to psychiatry than to most other medical disciplines, yet only about 2% of the research funds in the European Union are spent on mental health [327].

a) Positive life events (PLEs) predict decreases in neuroticism and negative life events (NLEs) increases in neuroticism;
b) PLE/NLE driven changes in neuroticism are long-lasting;
c) PLE/NLE driven changes in neuroticism are independent from life event driven changes in anxiety/depression;
d) Childhood adversity (before age 16) moderates the influence of NLEs/PLEs on neuroticism scores in adult life.

Chapter 3: Mutual Reinforcement between Neuroticism and Life Experiences

In this chapter I studied the magnitude and course of reciprocal associations between neuroticism and PLEs/NLEs in study of 296 Dutch individuals who were followed with five waves over 16 years (mean age at T_1= 34). I tested the following hypotheses:
a) Neuroticism levels are more predictive for variance in PLEs/NLEs than vice versa;
b) NLEs predict increases in neuroticism and higher neuroticism predicts more NLEs (a malignant cycle);
c) PLEs predict decreases in neuroticism and lower neuroticism predicts more PLEs (a benign cycle);
d) Increases in neuroticism after NLEs are less common than decreases after PLEs but more persistent.

Chapter 4: A Review of Environmental Influences on Neuroticism

In this chapter I reviewed environmental influences on neuroticism. To reduce genetic confounding, I focused on studies of monozygotic (MZ) twin pairs discordant for neuroticism. Additionally, I also reviewed longitudinal studies of within-individual change in neuroticism over intervals of at least one year. I confined myself to influences on neuroticism in the nuclear family (which comprises a romantic partnership), social network (Friends/Peers), occupational environments, and stressful life experiences, in adult population samples.

Chapter 5: Neuroticism and the Common Mental Disorders

In this chapter we reviewed the literature to evaluate available evidence bearing on the validity of five models that have been proposed to explain the link between neuroticism and the common mental disorders and to verify whether neuroticism is an independent etiologically informative risk factor. We reviewed the literature on confounding, operational overlap, stability and change, determinants, and treatment effects. The four studied models are:
a) The vulnerability model;
b) Spectrum model;
c) Common cause model;

d) The state model;
e) The scar model.

Chapter 6: Why Does Frustration Predict Psychopathology?

In this chapter I used data from the longitudinal Tracking Adolescents' Individual Lives Survey (TRAILS, n = 1158) to test four hypotheses about pathways that may underlie the prospective association between frustration (age 16) and psychopathology (age 19):

a) Stress generation (mediation via selection and evocation of stressful life events);
b) Heightened stress sensitivity (more psychopathology after events);
c) Cross-sectional frustration-psychopathology overlap ("carry-over");
d) A direct (non-mediated) effect of frustration.

Additionally, I explored whether high frustration predicts increases in internalizing and externalizing tendencies (mutually adjusted).

Chapter 7: Perceived Relationship Affection

Temperamental differences have been shown to select or evoke stressful life events, but we remain ignorant about the mechanisms that mediate this association. In this chapter we test whether differences in 'perceived relationship affection' accounted for part of the prospective association between temperament (*e.g.*, frustration) and stressful social event evocation in three social domains, *viz.* parents, peers, and romantic partners. We hypothesized that:

a) Individuals high (*vs.* low) on frustration experience (select/evoke) more subsequent stressful social events;
b) Prospective associations between frustration and subsequent stressful social events are partially mediated by perceived relationship affection;
c) Associations are domain-specific, *e.g.* perceived parental affection as the primary mediator of frustration-driven stressful social event evocation effects in the parental domain, and perceived peer affection as the mediator of frustration-driven stressful social event evocation effects in the peer domain;
d) Spill-over, *viz.*, associations between frustration and subsequent stressful social events in the romantic partner domain were mediated by either perceived parental affection or perceived peer affection.

Chapter 8: Relative Age Effects

I examined intra-classroom age position (or relative age) effects in adolescence on negative affective temperament (Fear and Frustration), and change in Fear and Frustration between age 11 and 16, as well as on depressive symptoms, physical development, and adolescents' school progress and performance (as rated by teachers) in TRAILS,

all adjusted for age at the time of measurement (*n*= 2230, mean age at baseline= 11.1, SD= 0.6, 51% girls). A demonstration of persistent relative-age effects in adolescence would show that childhood temperament is influenced by an (artificial) adult-imposed structuring of the environment that is bestowed upon them. I hypothesized that:

a) The relatively young adolescents showed unfavourable outcomes (relatively high Fear and Frustration) compared to the relatively old adolescents;
b) The relatively young showed different temperamental development between age 11 and 16 than the relatively old.

Chapter 9: Timing of Stressful Life Events Affects Stability and Change of Neuroticism

Data from the Finnish Twin Cohort (*n*= 21,085) was used to study the determinants of within-subject change in neuroticism over six years, while the timing of SLEs was taken into account. To control for confounding by shared genes and environments both within-twin pair and between-twin pair effects were tested for monozygotic and dizygotic twin pairs separately. Three hypotheses were tested:

a) Subjects who experienced stressful life events (SLEs) show an increase in neuroticism;
b) High baseline neuroticism moderated this effect;
c) Recent SLEs had a greater impact on neuroticism than distant SLEs.

Chapter 10: General Discussion

In the discussion I summarize, discuss, and integrate the research finding in the light of the known literature. I finish with suggestions for future research.